

# Sugarcane Farming, Occupational Solvent Exposures, and the Risk of Oral Cancer in Puerto Rico

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*The work history information from a population-based case-control study conducted in Puerto Rico was analyzed using a job exposure matrix to investigate the relationship between occupational exposures and cancers of the oral cavity or pharynx. After adjustment for age, alcohol, smoking, and residence in a logistic model, the risk for cancer of the oral cavity, but not the pharynx, was significantly elevated among farm workers in the sugarcane industry (OR = 4.4, 95% CI = 1.4–13.6). An exposure-response trend was seen for cumulative exposure to solvents, with an OR = 3.2 (95% CI = 0.8–12.6) in the highest exposure category. The overall contribution to the risk of cancer of the oral cavity or pharynx associated with occupational exposures in Puerto Rico appears to be small, however, the elevated risks were seen among sugarcane farmers and subjects with high cumulative exposure to solvents. (J Occup Environ Med. 2003;45:869–874)*

A population-based case-control study among residents of Puerto Rico was conducted to evaluate the reasons for the elevated rates of cancer of the oral cavity or pharynx.<sup>1</sup> A previous analysis of these data found that use of alcohol and tobacco were the major risk factors, accounting for approximately 76% of the cancers of the oral cavity or pharynx among men and 52% among women in Puerto Rico.<sup>2</sup>

Although the data are limited and often inconsistent, excess risks of oral cancer have been reported among plumbers, welders, metal workers, and electrical workers potentially exposed to high levels of metal dust or solvents.<sup>3–6</sup> In our study, information was collected on usual occupation, including the type of industry or service and the duration of employment. This work presents a detailed analysis of occupational risks for cancer of the oral cavity or pharynx in Puerto Rico, with special attention to the sugarcane industry, a major employer in Puerto Rico.

## Subjects and Methods

All incident cases of histologically confirmed cancers of the oral cavity or pharynx (ICD-9 codes 141, 143 to 146, 148, 149), excluding the lip (ICD-9 code 140), salivary glands (ICD-9 code 142), and nasopharynx (ICD-9 code 147), diagnosed among Puerto Rican residents aged 21 to 79 years between 1992 and 1995 were frequency matched on age, gender, and area of residence with population-based controls selected from two sources: a sampling frame of dwelling

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units for controls less than 65 and a listing of Medicare recipients for controls aged 65 and older, as previously described.<sup>2</sup> The study protocol was approved by Institutional Review Boards at the University of Puerto Rico and the U.S. National Cancer Institute and written informed consent was obtained from all study participants.

Interviews were completed for 367 (71%) of the oral cavity and pharyngeal cancer cases and 521 (83%) of the eligible controls. Excluded from the analysis were 25 cases with a histologic type consistent with a salivary gland origin. Information on tobacco and alcohol use, demographic characteristics, medical and dental history, as well as usual occupation, type of business, and duration of employment was sought from cases and controls by trained interviewers using a structured questionnaire in Spanish.

Usual occupation was coded using four-digit 1980 Standard Occupational Classification (SOC) codes.<sup>7</sup> The responses to questions about the type of company or product made were coded using four-digit 1987 Standard Industrial Classification (SIC) codes.<sup>8</sup> After review of the work history and the exclusion of 37 subjects with missing or invalid occupational history information, 699 males (286 cases and 413 controls) and 127 females (41 cases and 86 controls) were available for analysis. One additional male control was missing a specific occupation and was removed from analyses based on SOC codes.

Occupational exposures were assessed using three approaches. The first approach grouped two-digit SIC and SOC codes into seven broad industry and 12 broad occupation categories, respectively, that contained at least 10 cases and 10 controls. This analysis was conducted separately for males and females. The second approach merged four-digit SIC and SOC codes with similar types of exposures as assessed by an industrial hygienist (J.C.) to form 17 specific industry and 21 specific occupation groups, respectively, with at least 10 subjects or at least five cases. This analysis was

conducted for men only, because of the small number of women in these more specific categories.

The third approach used a job exposure matrix to classify relative exposure intensity, allowing for the investigation of exposure-response relationships. All unique four-digit SOC and SIC code combinations ( $n = 507$ ) were rated by an industrial hygienist (J.C.) with respect to potential for exposure to dusts (eg, carpenters, stone masons, excavation equipment operators), solvents (eg, painters, auto body repair shop, electronics repair technician), and metals (eg, welding and cutting, machinists, plating, and polishing). Exposure intensities for each of the three agents were rated on a four-point scale of 1, none; 2, low; 3, medium; and 4, high. These exposure ratings were assigned without knowledge of the case-control status of the subjects. To incorporate both duration and intensity of exposure, a cumulative exposure index as suggested by Xu et al<sup>9</sup> was created by crossing the job exposure matrix exposure intensity with the duration of employment in categories of <10 years, 10 to 20 years, and >20 years. Subjects with 10 or more years of employment in a job with high exposure levels or greater than 20 years of exposure in a job with medium exposure levels were classified in the high cumulative exposure category. Subjects employed less than 10 years in a job with high exposure, 10 to 20 years in a job with medium exposure, or greater than 20 years in a low-exposure job were assigned to the medium cumulative-exposure category. Subjects with less than 10 years in a job with medium exposure intensity or 20 or fewer years in a job with low-exposure intensity were assigned to the low cumulative-exposure group. Subjects who reported jobs with negligible exposure intensity were assigned no (0) exposure, regardless of duration.

Unconditional logistic regression models using the SAS PROC LOGIST procedure<sup>10</sup> were used to calculate

odds ratios (ORs) and 95% confidence intervals (CIs) for the occupation, industry, and exposure variables of interest. ORs were adjusted for age (<54, 55 to 59, 60 to 64, 65 to 69, 70 to 74,  $\geq 75$ ), residence (San Juan, other), gender (where appropriate), lifetime tobacco use (in six categories for males and three categories for females), and lifetime drinks of alcohol (in five categories for males and three categories for females). Several additional potential confounders (eg, education, income, and raw fruit and vegetable intake) were evaluated but were not included in the final model because they did not confound the relationship between occupational category and the risk of cancer of the oral cavity or pharynx. ORs were calculated for oral cavity and pharynx cancers combined, as well as separately for each site. ORs for specific SIC and SOC codes were also run based on duration of employment, but no consistent results were seen and thus are not shown. Tests for trends for the exposure indexes were obtained by assigning a score of 1, 2, and 3 to the low, medium, and high cumulative exposure categories, respectively, and treating this categorical variable as continuous in the logistic regression models.

## Results

No clear association was seen between cancer of the oral cavity or pharynx and the broad industry and occupational groups analyzed (Table 1). However, a nonsignificantly elevated risk of 2.8 (CI, 0.9–8.3) was observed for men employed in precision production occupations (eg, cabinet makers, shoemakers, butchers), and a significant risk was observed for women (OR, 5.4; CI = 1.1–27.3) but not men (OR, 0.7; CI = 0.4–1.2) in the wholesale/retail trade. Additionally, men in agriculture had a modest increase in risk (OR, 1.4; CI = 0.8–2.3), largely because of increased risk among sugarcane workers (OR, 2.2; CI = 0.9–5.3), especially sugarcane farmers (OR, 2.4; CI = 0.9–6.5; Table 2). Nonsignificant increased risks were also observed among electric services

**TABLE 1**

Risk of Oral Cavity or Pharyngeal Cancer in Puerto Rican Men and Women Associated with Usual Employment in Broad Industry and Occupation Categories Based on 2-Digit SIC and SOC Codes

Industry (SIC Codes)	Males			Females		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Agriculture (01–08)	60	64	1.4 (0.8–2.3)	–	–	–
Construction (15–17)	48	56	1.0 (0.6–1.7)	–	–	–
Manufacturing (20–39)	39	65	0.9 (0.5–1.5)	13	26	M0.6 (0.2–2.0)
Transportation/utilities (40–49)	28	42	1.0 (0.5–1.9)	–	–	–
Wholesale/retail trade (50–59)	42	72	0.7 (0.4–1.2)	6	4	5.4 (1.1–27.3)
Services (60–89)	42	66	1.4 (0.8–2.4)	10	21	0.8 (0.3–2.5)
Public Administration (91–97)	21	35	1.1 (0.5–2.2)	–	–	–
Occupation (SOC Codes)						
Executive, administrative, managerial (11–14)	10	12	1.6 (0.5–4.7)	–	–	–
Marketing and sales (40–4)	22	46	0.7 (0.3–1.3)	–	–	–
Administrative support (45–47)	8	28	0.5 (0.2–1.4)	5	8	3.7 (0.8–16.9)
Service (50–52)	26	44	1.2 (0.6–2.4)	9	9	2.1 (0.6–6.7)
Agricultural, forestry, fishing (55–58)	59	62	1.3 (0.8–2.3)	–	–	–
Mechanics and repairers (60–61)	20	23	1.3 (0.6–2.9)	–	–	–
Construction and extractive operations (63–65)	50	46	1.3 (0.8–2.3)	–	–	–
Precision production (67–69)	14	10	2.8 (0.9–8.3)	–	–	–
Production working (71–78)	22	48	0.8 (0.4–1.4)	7	22	0.3 (0.1–1.2)
Transportation, material moving (81–83)	27	45	0.6 (0.3–1.1)	–	–	–
Handlers, equipment cleaners, laborers (85–87)	11	19	0.4 (0.2–1.1)	–	–	–
Housewife	–	–	–	9	27	0.5 (0.2–1.5)

All risks relative to 1.0 for those of the same gender not in that usual industry or occupation. ORs adjusted for age, residence, smoking, and alcohol use in a logistic model. OR, odds ratio; CI, confidence interval.

industry workers (OR, 2.3; CI = 0.7–8.1), including electricians and others from the electric power industry (Table 2).

Risks for agricultural and sugarcane workers by anatomic subsite are presented in Table 3. Risks for all agricultural workers were similar for cancers of the oral cavity (OR, 1.4; CI = 0.8–2.6) and the pharynx (OR, 1.6; CI = 0.8–3.2). However, significantly elevated risks associated with employment in the sugarcane industry overall (OR, 3.4; CI = 1.2–9.4) and among sugarcane farmers or farm workers specifically (OR, 4.4; CI = 1.4–13.6) were observed for cancer of the oral cavity but not the pharynx (OR, 1.0 and 0.8, respectively). Among male sugarcane workers, the cases compared with controls tended to be younger (mean 66.0 versus 72.9 years), heavier drinkers (median 42.1 versus 21.0 drinks/week), and lighter consumers of fruit and vegetables (median 1.5 versus 2.0

**TABLE 2**

Risk of Oral Cavity or Pharyngeal Cancer in Puerto Rican Men Associated with Usual Employment in Selected Industry Categories Based on Four-Digit SIC Codes

Industry Category	Cases	Controls	OR (95% CI)
Agriculture: livestock	7	6	1.7 (0.5–6.4)
Agriculture: plants other than sugarcane	32	45	1.0 (0.5–1.8)
Agriculture: sugarcane	21	13	2.2 (0.9–5.3)
Sugarcane farmer and farm workers	17	10	2.4 (0.9–6.5)
Food and kindred products	11	13	1.3 (0.5–3.6)
Textile and apparel products	2	9	0.3 (0.1–2.3)
Lumber, wood, and furniture products	5	5	1.7 (0.3–9.5)
Metal products	10	12	1.0 (0.3–3.2)
Transportation	17	32	0.6 (0.3–1.2)
Electric services	7	8	2.3 (0.7–8.1)
Grocery stores	16	18	1.8 (0.7–4.4)
Eating and drinking places	13	18	1.0 (0.4–2.6)
Automotive repair shops	9	8	1.7 (0.5–6.5)
Hospitals and clinics	5	7	1.5 (0.4–6.0)
Educational services	6	16	1.4 (0.4–4.4)
Security	11	10	1.7 (0.5–5.6)
Misc. services	10	19	1.1 (0.4–2.9)
Misc. administrative, insurance, financial	20	44	0.8 (0.4–1.6)

All risks relative to 1.0 for men not in that selected industry. ORs adjusted for age, residence, smoking, and alcohol use in a logistic model. OR, odds ratio; CI, confidence interval.

**TABLE 3**

Risk of Oral Cavity or Pharyngeal Cancer in Puerto Rican Men Associated with Usual Employment in Agriculture and the Sugarcane Industry by Anatomical Site

Employment Group	(N = 413)	Oral Cavity (n = 174)		Pharynx (n = 112)	
	Controls	Cases	OR	Cases	OR
Agriculture industry	64	36	61.4 (0.8–2.6)	24	1.6 (0.8–3.2)
Sugarcane industry	13	16	3.4 (1.2–9.4)	5	1.0 (0.3–3.8)
Sugarcane farmers	10	14	4.4 (1.4–13.6)	3	0.8 (0.2–4.0)

All risks relative to 1.0 for men not in that industry or occupation. ORs adjusted for age, residence, smoking, and alcohol use in a logistic model. OR, odds ratio; CI, confidence interval.

servings per day), but had similar levels of smoking (median 20 cigarettes/day) and education level (<8 years). Male controls who worked in the sugarcane industry compared with all other male controls tended to be older (mean, 72.8 versus 61.2 years), heavier drinkers (median, 21.0 versus 8.7 drinks/week), heavier smokers (median, 20 versus 9 cigarettes/day), of lower social class (median education, <8 versus 8 to 11 years), and to have poorer diets (median intake of raw fruits and vegetables, 2.0 versus 3.7 servings/day). When stratified by lifetime alcohol consumption, the odds ratios were elevated in the lower as well as the upper strata, although the lower strata were based on small numbers (three cases, two controls).

Nonsignificant excesses of 3-fold or greater were noted for painters and plasterers (OR, 6.0); electricians and electrical workers (OR, 3.3); and plumbers, pipefitters, welders, and machinists (OR, 3.4; Table 4). There was a nonsignificant reduced risk (OR, 0.3) for men employed in the textile and apparel products industry.

The average duration of usual employment for all subjects was 26.1 years, with over 55% employed in their usual job for more than 20 years. However, the average duration of employment among sugarcane farmers was substantially longer, 33.9 years, with 81% reporting greater than 20 years of employment in the sugarcane industry.

Risks for cancer of the oral cavity or pharynx increased significantly with greater cumulative exposure to solvents, reaching 3.2 in the highest

**TABLE 4**

Risk of Oral Cavity or Pharyngeal Cancer in Puerto Rican Men Associated with Usual Employment Occupation Categories Based on Four-Digit SOC Codes

Occupation Category	Cases	Controls	OR (95% CI)
Food and beverage service workers	15	15	1.7 (0.6–4.3)
Farmers and farm workers	56	61	1.3 (0.8–2.3)
Mechanics and machinery maintenance	21	24	1.2 (0.6–2.6)
Construction workers and equipment operators	17	18	0.7 (0.3–1.7)
Carpenters and woodworkers	19	21	1.4 (0.6–3.3)
Brick and stone masons	8	9	1.1 (0.3–3.7)
Electricians and electrical workers	6	5	3.3 (0.8–14.6)
Painters and plasterers	6	1	6.0 (0.4–80.4)
Service: cleaning, housekeeping, childcare	5	19	0.6 (0.2–2.0)
Service occupations: security	5	8	1.6 (0.4–6.8)
Plumbers, pipefitters, welders, machinists	6	5	3.4 (0.7–16.0)
Truck drivers, transportation operators	23	34	0.6 (0.3–1.2)
Material-moving jobs	8	14	0.5 (0.2–1.4)
Assemblers and hand working occupations	4	6	0.7 (0.1–3.3)
Production supervisors, inspectors	7	17	0.8 (0.3–2.3)
Executives, administrators, financial managers	10	12	1.6 (0.5–4.7)
Engineers, scientists, technical professions	7	7	2.3 (0.6–7.8)*
Social, religious, legal, teaching professions	4	15	0.7 (0.2–2.6)
Sales and related occupations	22	46	0.7 (0.3–1.3)
Administrative, clerical and general office jobs	8	28	0.5 (0.2–1.4)
Production machinery operation	9	23	0.7 (0.3–1.7)

All risks relative to 1.0 for men not in that selected occupation. ORs adjusted for age, residence, smoking and alcohol use in a logistic model.

\* OR adjusted for age, residence, and alcohol use in a logistic models; controls in this cell did not smoke.

OR, odds ratio; CI, confidence interval.

exposure category (p for trend, 0.03, Table 5). There was a nonsignificant trend of increased risk with greater cumulative exposure to metals. No gradient in risk was observed across dust exposure categories.

## Discussion

In this population-based case-control study of cancer of the oral cavity and pharynx in Puerto Rico, we found a 4-fold significantly elevated risk limited to cancer of the oral cavity among farmers and farm workers in

the sugarcane industry. Sugarcane farming was among the most frequently reported occupations within this population, with a relatively large number of subjects in our study working in the sugarcane industry (n = 34), predominantly as sugarcane farmers (n = 27). The sugarcane industry, found mostly in developing countries,<sup>11</sup> is also a major employer in Puerto Rico as well as in Florida, Louisiana, and Hawaii in the United States. Before the recent introduction of mechanized harvesting equipment,

**TABLE 5**  
Risk of Oral Cavity or Pharyngeal Cancer in Puerto Rican Men by Cumulative Exposure to Dusts, Metals and Solvents Based on a Job-Exposure Matrix

Agent	Cumulative Exposure	Cases	Controls	OR (95% CI)	P Value for Trend
Dusts	None	119	197	1.0	0.5
	Low	25	51	0.5 (0.3–1.0)	
	Medium	60	70	1.3 (0.7–2.1)	
	High	82	94	1.1 (0.7–1.7)	
Metals	None	234	350	1.0	0.2
	Low	20	23	1.1 (0.5–2.6)	
	Medium	24	32	1.2 (0.6–2.5)	
	High	8	7	2.7 (0.7–10.6)	
Solvents	None	205	321	1.0	0.03
	Low	28	33	1.0 (0.5–2.1)	
	Medium	41	54	1.6 (0.9–2.9)	
	High	12	4	3.2 (0.8–12.6)	

All risks relative to 1.0 for men not exposed to each agent. ORs adjusted for age, smoking, and alcohol use in a logistic model. OR, odds ratio; CI, confidence interval.

sugarcane was generally cut by hand.<sup>12</sup> The sugarcane stalk is 85% juice by weight, and when chewed, may cause abrasions leading to traumatic lesions of the oral mucosa. Sugarcane workers may be exposed to airborne spores of the thermophilic actinomycetes, *Thermoactinomyces sacchari*, a bacterium responsible for bagassosis, a hypersensitivity pneumonitis affecting sugarcane mill workers exposed to dried bagasse (fibers that remain after extraction of sugarcane juice).<sup>11,13</sup> Although not known to cause oral cavity cancer, exposure to actinomycetes has been associated with chronic destructive granulomas or ulcers of the mouth.<sup>14</sup> Some studies of sugarcane workers have reported an increased risk of lung cancer and mesothelioma,<sup>15–18</sup> which may result from exposures to biogenic amorphous silica (BAS) fibers during harvesting<sup>15,19</sup> or to asbestos or crystalline silica in processing facilities.<sup>15,17</sup> The possible role of BAS fibers in cancer of the oral cavity is suggested also by the elevated rates of esophageal cancer in areas of China and Iran,<sup>20,21</sup> where BAS fibers are ingested in flour and millet. Sugarcane fields are burned immediately prior to harvesting to remove dead leaves that otherwise impede the harvest and interfere with sugar extraction from the stalks during processing. Thus, sugarcane workers

are exposed to the residues from the combustion of organic debris that contain polyaromatic hydrocarbons.<sup>19</sup> In addition, sugarcane farmers are exposed to various pesticides, particularly organophosphates, carbamates, and pyrethroids, as well as herbicides.<sup>11</sup>

Despite adjustments made in the analysis, it is possible that the elevated risk of cancer of the oral cavity in sugarcane farmers results, at least in part, from residual confounding by the major lifestyle risk factors, particularly high intake of alcohol, low intake of fresh fruits and vegetables, and low socioeconomic status, that are prevalent in sugarcane workers.<sup>2,5,22–24</sup> However, the risk of oral cavity cancer among sugarcane farmers was elevated among both light and heavy drinkers, suggesting that factors other than alcohol may contribute to occupational causation. Another possible confounder is selection bias; the mean age of the sugarcane worker controls was substantially older than other controls, so that our use of a dwelling unit-based sampling scheme may have under-ascertained younger sugarcane workers (<65 years of age) who were more likely to be migrant harvesting workers<sup>15</sup> with transient and/or substandard living conditions.<sup>25</sup> Further studies of cancer of the oral cavity in areas with a concentration of sugarcane workers, particularly in develop-

ing countries where harvesting is still performed by hand, are needed to replicate these findings.

Our study also revealed a significant dose-response trend in the risk of cancer of the oral cavity or pharynx across cumulative solvent exposure categories that reached 3-fold in the high exposure category. Although we can not evaluate risks for specific solvents, the 12 cases in the high-exposure group were employed as painters,<sup>4</sup> cabinet makers,<sup>4</sup> or workers in automobile body and repair and paint shops.<sup>4</sup> These occupations have a high probability of exposure to solvents (eg, toluene, xylene, benzene), formaldehyde, or other organic compounds that have previously been linked to oral cancer.<sup>4,26–28</sup>

Furthermore, nonsignificantly increased risks of 2-fold or greater were seen for certain industries and occupations (ie, electric services; electricians, electrical workers; painters, plasterers; plumbers, pipefitters, welders, machinists), as reported in some previous studies,<sup>3–6,29,30</sup> but not others.<sup>5,31</sup> The nonsignificantly reduced risk (OR, 0.3) associated with employment in the textile and apparel products industry is consistent with findings from a large case-control study in the United States<sup>5</sup> but not in a case-referent study in Italy.<sup>4</sup> The significantly elevated risk (OR, 5.4) for females in wholesale/retail trade, based on only six cases and four controls, is probably due to chance, since the risk for men employed in that industry was reduced.

Although exposure to dusts (eg, metal, wood, and cement) has been linked to oral cancer in some previous studies,<sup>28,29,32</sup> we found no excess risk using an index of cumulative dust exposure. The trend for cumulative exposure to metals was equivocal due to the small number of subjects in the high exposure category (OR, 2.7), largely reflecting the elevated risks for machinists and welders.

Our study was limited by the difficulty in accurately assessing occupational exposure through interviews in case-control studies using occupational coding systems established

for economic analysis and not for exposure assessment. Although the more specific four-digit SIC and SOC groupings provide greater homogeneity in exposure within groups, and greater contrast between groups than the broad two-digit SIC and SOC groupings, the smaller number of subjects per group and the increased number of comparisons may lead to less stable risk estimates and spurious findings. The use of a job exposure matrix based on combinations of industry and occupation and duration of employment should enhance the power of a case-control study to identify etiologic agents by grouping jobs with similar exposures; however, our analysis was based only on usual job reported. Although most subjects were employed in their usual job for more than 20 years, it is likely that some subjects spent significant periods of time in other occupations.

In summary, this population-based case-control study in Puerto Rico evaluated risks for cancer of the oral cavity or pharynx associated with usual employment in a variety of occupations and industries as well as cumulative exposure to dusts, metals, and solvents. After adjustment for alcohol and tobacco use, occupational exposures contributed only slightly to the risk of these cancers. However, the elevated risks among sugarcane farmers and farm workers, and among workers with solvent exposures, warrant further investigation in appropriate populations.

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